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09/19/2006

John D. Fikes

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EXAMINER

DAVIS, MINH TAM B

ART UNIT

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/553,703	<b>Applicant(s)</b> FIKES ET AL.	
	<b>Examiner</b> MINH-TAM DAVIS	<b>Art Unit</b> 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 25 November 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 15-40 is/are pending in the application.
- 4a) Of the above claim(s) 16-21, 27-28, 32, 34-35, 37-40 is/are withdrawn from consideration.
- 5) ☒ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15, 22-26, 29-31, 33 and 36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***DETAILED ACTION***

Applicant's election with traverse of Group A, claims 15, 22-26, 29-31, 33, 36, a method for treating breast cancer in the reply filed on 11/25/08 is acknowledged.

The traversal is on the ground(s) that: 1) Group A should contain claims 34-35 because they both depend on claim 33, and 2) the claims of group A should not be limited to breast cancer.

This is not found persuasive because of the following reasons:

1) Claims 34-35 belong to groups G and H, and not group A. Delaying recurrence of cancer as claimed in claim 34 and preventing metastasis of a primary tumor as claimed in claim 35 belong to a method of preventing a cancer of groups G and H, which is a different process than a method of treating a cancer of claim 33, because they do not share the same objectives. The method of group G is an additional use of the combination of peptides of group A, and the method of group H does not use the combination of peptide of group A. If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims. After that, all other products and methods will be broken out as separate groups. See PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b) and (d).

2) Different target treated cancers belong to different methods, because they are different products, and do not share the same etiology and characteristics.

The requirement is still deemed proper and is therefore made FINAL.

In a telephonic conversation with the Attorney Paul Calvo on 01/06/09, Applicant elects the combination of SEQ ID NO: 1, SEQ ID NO:2 and SEQ ID NO:3.

**Accordingly, Group A, claims 15, 22-26, 29-31, 33, 36, the combination of SEQ ID NO: 1, SEQ ID NO:2 and SEQ ID NO:3, and a method for treating breast cancer are examined in the instant application.**

The embodiment of claims 15, 22-26, 29-31, 33, 36, as drawn to a composition comprising SEQ ID NOs 5-10, and a method for treating a cancer other than breast cancer has been withdrawn from consideration as being drawn to non-elected invention. Claims 16-21, 27-28, 32, 34-35, 37-40 are withdrawn from consideration as being drawn to non-elected invention.

***Claim Rejections - 35 USC § 112, First Paragraph, Scope***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 22-26, 29-31, 33, 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a combination of the CTL peptides consisting of SEQ ID NO: 2, SEQ ID NO:3 and SEQ ID NO:4, and the PanDR binding peptide consisting of SEQ ID NO:1, does not reasonably provide enablement for 1) a composition comprising at least three peptides, each of said three peptides is less than **15 amino acids** and **comprises** a CTL epitope and/or analog of SEQ ID NO: 2, SEQ ID NO:3 and SEQ ID NO:4, and further comprising an additional peptide of less than **25 amino acids comprising** a helper T cell epitope, the PanDR binding peptide of SEQ ID NO:1, and 2) a method for **treating breast cancer**, using

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the CTL peptides of SEQ ID NO: 2, SEQ ID NO:3 and SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

To comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must enable one skilled in the art to make and use the claimed invention without undue experimentation. The claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 ( Fed.Circ.1988 ) as follows: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The specification discloses that breast cancer cells express the proteins CEA, p53, MAGE 2/3, Her 2/neu (table 5 on page 121) and contemplate the use a combination of CTL epitopes from these proteins for treating cancer (para 304 on page ). The specification discloses that from a combination of 10 different CTL peptides and analogs (EP2101) administered into HLA-A2.1/Kb transgenic mice, the fixed-anchor analog peptide CEA.24V9 (SEQ ID NO: 4), the heteroclitic analog CEA.691H5 (SEQ ID NO:9), the fixed anchored analog HER-2/neu.369V2V9 (SEQ ID NO:7), the wild type MAGE-2.157 (SEQ ID NO:3), and the heteroclitic analog MAGE-3.11215 (SEQ ID NO: 10) induce strong CTL response, and the remaining of the 10 peptides induce weak CTL response (Example 13 on p.89, table 1 on page 109 for identification of different peptides). It is noted that the transgenic mice do not have

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breast cancer. The specification discloses that SEQ ID NO:4 is a fixed-anchored **analog** from a CTL peptide of CEA protein, while SEQ ID NO:2 and SEQ ID NO:3 are wild type CTL peptides from HER-2/neu and MAGE-2 proteins, respectively (Table 1 on page 109).

The specification does not have any data or objective evidence that a peptide of less than 15 amino acids and comprises a CTL epitope of SEQ ID NO: 2, SEQ ID NO:3 or SEQ ID NO:4 would induce CTL activity. The specification does not have any data or objective evidence that a peptide of less than 25 amino acids and comprising a helper T cell epitope, the PanDR binding peptide of SEQ ID NO:1 would have the activity of SEQ ID NO:1. The specification does not have any data or objective evidence that breast cancer is successfully treated using a combination of SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4.

**1.** Claims 15, 22-26, 29-31, 33, 36 are rejected under 112, first paragraph, for lack of enablement for: 1) a peptide of **less than 15 amino acids** and comprises a CTL epitope and/or analog of SEQ ID NO: 2, SEQ ID NO:3 or SEQ ID NO:4, and 2) a peptide of less than 25 amino acids and comprising a helper T cell epitope, the PanDR binding peptide of SEQ ID NO:1.

A peptide of less than 15 amino acids and comprises a CTL epitope of SEQ ID NO: 2, SEQ ID NO:3 or SEQ ID NO:4 encompasses peptides of up to 14 amino acids and comprising the nine amino acids of SEQ ID NO: 2, the ten amino acids of SEQ ID NO:3 or the nine amino acids of SEQ ID NO:4. A peptide of less than 25 amino acids and comprising a helper T cell epitope, the PanDR binding peptide of SEQ ID NO:1 encompasses peptides of up to 24 amino acids and comprising the thirteen amino acids of SEQ ID NO: 1.

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One cannot predict that a peptide of less than 15 amino acids and comprises a CTL epitope of SEQ ID NO: 2, SEQ ID NO:3 or SEQ ID NO:4 could still induce a CTL response, because one cannot predict the effect of surrounding amino acids on the function of the CTL epitope of SEQ ID NO: 2, SEQ ID NO:3 or SEQ ID NO:4. One cannot predict that the claimed sequences could bind to MHC and elicit T cells response, due to **the unpredictable effect** on MHC binding, and/or CTL recognition or activation **of unknown flanking sequences**, which effect could also depend and/or vary with the size of the amino acid sequence added to the CTL epitope. Bergmann et al, 1994 (J Virol, 68(8): 5306-5310) teach that CTL recognition of a 9 amino acid CTL epitope of the nucleocapsid protein (JN), even having immediate flanking sequences composed of its native sequence, varies, and depends on the size and/or composition of the flanking sequences (abstract , figures 1-2 on page 5307). For example, the longest sequence vtan 38 is most recognized as compared to the smaller sequences vtan 7, or vtan 2 (figures 1-2 on page 5307). Eisenlohr et al, 1992 (J Exp Med, 175: 481-487) teach that flanking sequences influence the presentation of a CTL peptide. Eisenlohr et al teach that addition of just two C-terminal native amino acids or ten native amino acids at the N- and C-termini all abolishes the CTL recognition (abstract, p. 484). Eisenlohr et al teach that any one or a combination of the following could be involved in the negative effects of flanking sequences: 1) Sequestration of the peptides on peptide binding proteins in the cytosol or exocytic compartment, 2) Inability of peptide intermediates to be transported from the cytosol to the exocytic compartment, 3) Inability of peptide intermediates to associate with accessory molecules that might function to deliver peptides to Class I molecule in the exocytic compartment, or 4) Inability of cellular proteases to generate antigenic peptide from the protein or longer peptide (p. 485, first column, last

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paragraph). Shastri et al, 1995 (J Immunol, 155: 4339-4346) teach that presentation of CTL peptide is profoundly influenced by specific added C-terminal flanking residues. Shastri et al teach that of the five amino acids C, I, L, M, V that can serve as C-terminal anchors, three amino acids C, I, L are actually inhibitory to CTL recognition (p. 4343, first column). Shastri et al further teach that the extra amino acid could result in either an intervening bulge, or the flanking residue projecting out, and the accessibility to the carboxypeptidases could be affected, resulting in the low yield to processed antigenic CTL peptide (p. 4345, second paragraph). Guo et al, 1992 (Nature, 360: 364-366) teach that different length peptides bind to a HLA molecule similarly at their ends but bulge out in the middle. Thus in view of the teaching in the specification and in the art, one cannot predict that addition of unknown amino acids to the claimed SEQ ID NO: 2, SEQ ID NO:3 and SEQ ID NO:4 would not result in losing CTL recognition, or binding affinity to MHC molecule due to the intervening bulging effect at the middle of the molecule, or the flanking residue(s) projecting out, and/or the loss of the accessibility to the carboxypeptidases.

Similarly, one cannot predict that a peptide of less than 25 amino acids and comprising a helper T cell epitope, the PanDR binding peptide of SEQ ID NO:1 would have the activity of SEQ ID NO:1, in view of the above teaching of Bergmann et al, Eisenlohr et al, Shastri et al, and Guo et al, *supra*.

**2. Claims 33, 36 are also rejected under 112, first paragraph, for a method for treating breast cancer.**

Although CTL activity could be induced in transgenic mice without breast cancer burden, one cannot predict that CTLs could be induced in a subject having breast cancer, due to the well

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known immuno-suppression by cancer cells, and that breast cancer could be successfully treated using a combination of SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4, due to the unpredictability of cancer immunotherapy. It is well known in the art that cancer immunotherapy is highly unpredictable. Mellman I, 2006, *The Scientist*, 20(1): 47-56, teaches that immunotherapy of cancer has yet to live up to expectations (p.47). Mellmann teaches that attempts at using cytokines to stimulate anticancer T cells, or deploying toxin-conjugated antibodies as magic bullets were never quite successful, and that therapeutic vaccines for cancer have proven similarly disappointing (p.47). Moreover, antigen internalization or downregulation can cause repeat dosing to be unsuccessful due to the disappearance of the antibody target (p.126, paragraph before last). Furthermore, Kaiser (*Science*, 2006, 313, 1370) teaches that 90% of tumor drugs fail in patients, see 3<sup>rd</sup> col., 2<sup>nd</sup> to last para. Furthermore, cancer tolerance is a well known phenomenon. Boon, 1992 (*Adv Can Res*, 58:177-210) teaches that for active immunization in human patients we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have occurred and it may prevent immunization and several lines of evidence suggest that large tumor burdens can tolerize or at least depress the capability to respond against the tumor (p. 206, para 2). In addition, Boon teaches that even if activated CTLs are significantly increased, the therapeutic success remains unpredictable due to inconsistencies in antigen expression or presentation by tumor cells, such as loss of tumor antigen (p.198, first paragraph). Kirkin et al, 1998, *APMIS*, 106 : 665-679, teach that although several peptides of melanoma associated antigens have been identified as recognized by CTL in vitro, and in particular peptides from MAGE-A1 and MAGE-A3 have been tested for their ability to induce anti-melanoma immune

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response in vivo, so far only one of the peptides, peptide EVDPIGHL Y of MAGE-A3, has limited anti-tumor activity, indicating their low immunogenicity (p.666, second column, second paragraph, last 6 lines). Smith RT, 1994 (Clin Immunol, 41(4): 841-849), teaches that antigen overload, due to antigen shedding by actively growing tumor, could block specifically either cytotoxic or proliferative responses of tumor specific T cells (p. 847, last paragraph bridging p.848 and p.848). Smith further teaches that many tumors progressively lose MHC representation at the surface of the cell, and the loss of surface Class I MHC could severely limits the possibilities for cytotoxic T cells specific for a tumor specific antigen to find said tumor specific antigen in the necessary MHC context (p.484). Bodey et al, 2000, Anticancer Res, 20: 2665-2676, confirm the teaching of Boon and Smith, by explaining the reasons for failure of vaccine in human. Bodey et al teach that although general immune activation against the target antigens has been documented in most cases, reduction of tumor load has not been frequently observed in human patients (abstract, second column, p.2673). Bodey et al teach that the failure of cancer vaccine is due to natural selection of highly aggressive clones in the treated patient, said clones no longer express the cancer specific antigen (abstract, second column, p.2673). Bodey et al teach that these clones of tumor cells survive the immune system, through secretion of immunoinhibitory cytokines, downregulation of MHC, loss of costimulatory molecules, and induction of T cell anergy (p.2673, second column, last paragraph). Similarly, Lee et al, 1999, J Immunol, 163: 6292-6300, teach that although a quantifiable T-cell specific immune response is detected in melanoma patients, such a response does not associate with regression of metastatic melanoma (abstract, and Discussion on pages 6297-6299).

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MPEP 2164.03 teaches that “the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling.”

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, there would be an undue quantity of experimentation required for one of skill in the art to practice the claimed invention, that is commensurate in scope of the claims.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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Claims 15, 22-26, 29-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Fikes et al, US 6,602,510 B1, filed on 04/05/2000.

Claims 15, 22-26, 29-30 are as follows:

15. (new) A composition comprising at least three peptides, wherein each of said three peptides is less than 15 amino acid residues in length and comprises a cytotoxic T- cell lymphocyte (CTL) epitope and/or analog selected from the group consisting of:

RLLQETELV (SEQ ID NO:2),

YLQLVFGIEV (SEQ ID NO:3), and

LLTFWNPPV (SEQ ID NO:4).

22. (new) A composition according to claim 15, further comprising an additional peptide, wherein said additional peptide is less than 25 amino acid residues in length and comprises an helper T lymphocyte (HTL) epitope.

23. (new) A composition according to claim 22, wherein said additional peptide is a PanDR binding peptide.

24. (new) A composition according to claim 23, wherein said Pan DR binding peptide comprises the amino acid sequence aKXVAAWTLKAAa (SEQ ID NO: 1).

25. (new) A composition according to claim 15, further comprising a liposome.

26. (new) A composition according to claim 15, further comprising a lipid.

29. (new) A composition according to claim 15, further comprising a pharmaceutical excipient.

30. (new) A composition according to claim 29, wherein said pharmaceutical excipient is an adjuvant.

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Fikes et al teach a composition comprising at least two antigens from CEA, HER2/neu, MAGE-2, MAG-3 and p53, or at least two, **three**, or up 19 or more epitopes from Table 6 (column 6, first paragraph). Table 6 on columns 57-58 teaches identified CTL epitopes from CEA, p53, Her2/neu, MAGE-2 and MAGE-3 for A2 vaccine, among which epitopes are the CEA epitope of SEQ ID NO:22, the Her2/neu epitope of SEQ ID NO:7 and the MAGE-2 epitope of SEQ ID NO:6, which is the same as the claimed **SEQ ID NO: 4, SEQ ID NO:2 and SEQ ID NO: 3**, respectively. Fikes et al teach that four tumor-associated antigens, CEA, p53, MAGE2/3 and HER2/neu are expressed in various tumor types, and that a vaccine comprising **epitopes among these four tumor associated antigens** would induce CTL response against several major cancer types (column 39, 4<sup>th</sup> paragraph, Table 7 on columns 57-58). Thus, the teaching of Fikes et al encompasses **any combination** among the CTL epitopes of the four tumor associated antigens cited in table 6. Fikes et al teach that the ability to induce CTL of the vaccine can be enhanced by adding at least one HTL epitope, such as Pan-DR-binding peptide, which peptide has the same structure as the claimed **SEQ ID NO:1** (column 33, item IV,J.2). Fikes et al teach that the peptides can be conjugated to **lipids** to prime CTL response, and that the vaccine could include an **adjuvant**, such as aluminum hydroxide (column 28, paragraph before last). Fikes et al teach that the peptides can also be administered via **liposomes**, which serve to target the peptides to a particular tissue, as well as to increase the half life to the peptides (column 37, lines 23-27).

Although the reference does not explicitly teach a combination of SEQ ID NO:1, SEQ ID NO: 2, SEQ ID NO: 3 and SEQ ID NO:4, however, the claimed composition appears to be the same as the prior art vaccine composition. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does

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not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fikes et al, US 6,602,510 B1, filed on 04/05/2000, in view of Reed et al, US 6,432,707 B1, filed on 06/22/2000.

Claim 31. (new) A composition according to claim 30, wherein said adjuvant is a mineral oil adjuvant.

The teaching of Fikes et al has been set forth above.

Although Fikes teach aluminum hydroxide adjuvant, Fikes et al do not teach mineral oil adjuvant.

Reed et al teach that most adjuvant contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil (column 52, last paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to replace the aluminum hydroxide adjuvant taught by Fikes et al with the mineral oil adjuvant taught by Reed et al, because they all are adjuvant that protects the antigen from rapid catabolism.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830.

The examiner can normally be reached on 9:00 AM-5:30 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS

January 14, 2009

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643